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EDITORIAL COMMENT

Management of Myocardial Infarction: Looking Beyond Efficacy*

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Over the last two decades, management of acute myocardial infarction (MI) has shifted from a "wait and watch" strategy to an increasingly aggressive strategy of restoring and maintaining (e.g., thrombolytics, antiplatelet agents) early patency to the infarct-related vessel and to other approaches that directly protect the myocardium (e.g., beta-blockers, angiotensin-converting enzyme inhibitors). Improved outcomes in MI have been achieved largely by using a combination of simple pharmacologic therapies and by the introduction of specialized coronary care units (1). In recent years advances in catheter based technologies have improved reperfusion success in MI patients with ST elevation. Randomized clinical trials of primary balloon percutaneous transluminal coronary angioplasty (PTCA) versus thrombolytic therapy have demonstrated that primary PTCA results in higher rates of coronary patency and lower rates of stroke, reinfarction and death (2). However, the relative benefit of PTCA over thrombolytic therapy is still unknown in a community setting in which access to catheterization laboratories (cath labs) and operator expertise is less uniform than in the trial setting (3). Whether immediate availability of invasive facilities, compared with referral of sick or high-risk patients to offsite cath labs, will improve outcomes is not known. This question has important medical, organizational, cost and training implications.

Rogers et al. (4) attempt to answer this question using

See page 371

data from a large registry of 1,506 U.S. hospitals that represent a spectrum of hospital types (noninvasive, cath-capable, PTCA-capable, coronary artery bypass graft-capable) and regions. They observed that the time to thrombolytic therapy was similar among the four types of hospitals and, as expected, that a greater proportion of patients initially presenting to hospitals capable of cardiac catheterization received invasive therapy but a greater proportion of those admitted to noninvasive centers was transferred. However, the primary mode of reperfusion was still thrombolytic therapy in each of the four categories of patients. One would expect that availability of immediate PTCA would allow additional patients not eligible for thrombolytic therapy to receive a catheter based intervention. However, the overall rates of reperfusion attempts were not significantly different among the four types of hospitals, and the risk profiles of the patients receiving reperfusion treatment (i.e., either thrombolytic or PTCA) treated in hospitals with and without PTCA facilities were similar. Consequently in the approximately 10% of patients for whom out-of-hospital data are available, 90-day survival after discharge was not significantly different whether or not invasive facilities were available. Although the follow-up data are limited and only short-term, they are consistent with the hypothesis that the initial management of MI does not differ whether or not invasive facilities are available on site. This is consistent with other studies that show that availability of catheterization facilities does not broaden the types or increase the risk profiles of patients to be treated (5). Paradoxically, lower risk patients are more often selected to undergo catheterization. This bias reduces the potential benefits of invasive therapies, first by subjecting lower risk patients to a therapy they may not necessarily need—thereby resulting in higher peri-procedural complications (major bleeds, strokes and mortality)—and second, by not delivering the most aggressive care to the highest risk patients, who stand to benefit the most.

Before embarking on newer and more costly treatment strategies, perhaps efforts should be directed at optimizing the use of proven therapies. Such an approach is more likely to lead to a greater benefit. For instance, the average time to thrombolytic therapy across all hospital groups in this study (42 min) is still longer than recommended (1,6). Efforts should be directed at continuously monitoring this variable and providing these data to local physicians at each center in an effort to improve the performance of those providing first-line therapy. Emergency personnel should also be appropriately trained in the early recognition of those patients who are at high risk and require immediate transfer to a facility with invasive capability. This will improve the selection for those patients who require invasive management and therefore improve the impact of these therapies. Although there may be, at best, modest benefits of one thrombolytic agent versus another (e.g., tissue plasminogen activator vs. streptokinase), the most important determinant

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of outcome is not which agent to use but, rather, whether a thrombolytic agent is indicated and, if so, how soon it is administered. Newer data, with combinations of thrombolytic agents and platelet GPIIb/IIIa receptor inhibitors or bolus administration of new generation thrombolytics, suggest that 90-min patency rates may be enhanced and approach those achieved with primary PTCA (7,8). However, these therapies are limited by the higher rates of intracranial bleeds and their high costs (both direct and indirect). In contrast, previous data from several sources indicate underutilization of proven and less expensive therapies (e.g., aspirin, beta-blockers or lipid lowering).

The study by Rogers et al. (4) does not distinguish between the management of MI patients presenting with and without ST elevation on the initial electrocardiogram. Patients without ST elevation MI tend to be older, have higher rates of three-vessel disease, diabetes and previous MI and consequently have higher mortality and heart failure. Unlike MI with ST elevation, it may be more difficult to identify the culprit lesion, and thrombolytic therapy has been shown to worsen outcome. Supporters of an invasive strategy argue that there are several benefits to catheterization, including: 1) early identification of surgical disease, including left main lesions; 2) early identification of non-coronary disease, so that the risks of prolonged antithrombin or antiplatelet therapy can be reduced; 3) potential cost savings in terms of hospital length of stay; and 4) reduced angina. However, studies randomizing patients to routine early catheterization versus selective catheterization based on failure of medical management or spontaneous ischemia do not show a significant benefit in terms of death or MI in favor of the invasive arm (9,10). Indeed some studies indicated a worse outcome (10). In the two studies that suggested a long-term benefit of death and MI in the invasive strategy (11,12), the intervention was either selective or was performed a few days or even weeks later, thus allowing the patient to be first stabilized medically.

Substantial improvements in the management of MI patients will result from organizational and system changes that lead to rapid and more widespread use of proven and relatively simple therapies (i.e., improving patient recognition of chest pain, early presentation to emergency room, improving door to needle time of thrombolytic therapy and use of early aspirin, beta blockers and angiotensin-converting enzyme inhibitors in appropriate patients). A small change in these factors (e.g., a 10-min decrease in door to needle time across the U.S. or a 10% increase in use of aspirin, beta blocker, or lipid lowering therapy) is likely to have a large beneficial effect in improving outcomes of MI patients (13).

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